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DATE: Wednesday, June 04, 2003

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DB=USPT,PGPB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L9	L8 and (ER or RXR or RAR)	11	L9
L8	l1 and (transgen$ or knockout)	51	L8
L7	L6 not l4	9	L7
L6	l1 and ER	12	L6
L5	L4 not l3	1	L5
L4	l1 and RXR	3	L4
L3	l1 and RAR	2	L3
L2	L1 near3 RAR	0	L2
L1	Cre near3 (fus$ or ligat$)	69	L1

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NEWS 17 Dec 17  TOXCENTER enhanced with additional content
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NEWS 24 Feb 26  NTIS now allows simultaneous left and right truncation
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NEWS 26 Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results
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NEWS 29 Mar 24  Additional information for trade-named substances without
          structures available in REGISTRY
NEWS 30 Apr 11  Display formats in DGENE enhanced
NEWS 31 Apr 14  MEDLINE Reload
NEWS 32 Apr 17  Polymer searching in REGISTRY enhanced
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          added to PHAR
NEWS 37 May 15  MEDLINE file segment of TOXCENTER reloaded
NEWS 38 May 15  Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39 May 16  CHEMREACT will be removed from STN
NEWS 40 May 19  Simultaneous left and right truncation added to WSCA
NEWS 41 May 19  RAPRA enhanced with new search field, simultaneous left and
          right truncation

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          MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
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=> s Cre (3a) (fus? or ligat?)
L1        218 CRE (3A) (FUS? OR LIGAT?)

=> s l1 and (RXR or RAR or ER)
L2         37 L1 AND (RXR OR RAR OR ER)

=> s l2 and (transgen? or knockout)
L3         26 L2 AND (TRANSGEN? OR KNOCKOUT)

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L4         12 DUP REM L3 (14 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 12 ANSWERS - CONTINUE? Y/(N):y

L4  ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2003 ACS
AN  2002:511498  CAPLUS
DN  137:42577
TI  A  ***transgenic***  mouse carrying a gene for a  ***cre***
    recombinase  ***fusion***  protein regulated by synthetic estrogens
IN  Chambon, Pierre; Metzger, Daniel
PA  Association pour le Developpement de la Recherche en Genetique Moleculaire
    Aderegem, Fr.
SO  Fr. Demande, 141 pp.
    CODEN: FRXXBL
DT  Patent
LA  French
FAN.CNT 1
    PATENT NO.      KIND  DATE        APPLICATION NO.  DATE
    --------------- ----  ----------  ---------------  --------
PI  FR 2814642      A1    20020405    FR 2000-12570    20001003
    US 2002100088   A1    20020725    US 2001-853033   20010511
    WO 2002028175   A2    20020411    WO 2001-IB2248   20010928
    WO 2002028175   A3    20030109
      W: CA, JP
      RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
          PT, SE, TR
PRAI FR 2000-12570    A    20001003
    US 2001-853033    A    20010511
AB  A  ***transgenic***  non-human metazoan, specifically a mouse, that
    carries the gene for a  ***fusion***  protein of  ***cre***
    recombinase and a nuclear estrogen receptor is described. The receptor is
    responsive to synthetic estrogens, such as tamoxifen, but not to natural
    estrogens and so can be used to regulate recombination via loxP sites,
    e.g. at different developmental stages, allowing the anal. of the role of
    a gene at these stages. Specifically, the method is used to investigate
    the function of retinoid X receptor .alpha. (  ***RXR***  .alpha.). The
    construction of the genes for  ***RXR***  .alpha. contg. loxP sites and
    the  ***Cre***  recombinase  ***fusion***  protein with an estrogen
    receptor is described. The fusion protein gene was placed under the
    control of tissue-specific promoters to limit the deletions to specific
    tissues.  ***Transgenic***  mice carrying these genes were constructed
    by std. methods. Inactivation of the  ***RXR***  .alpha. gene in the
    epidermis resulted in alopecia and the development of cysts on the skin
    within 6-12 wk of administration of tamoxifen. The skin continued to
    degenerate and after 20 wk small wound-like lesions appeared.
    Inactivation of the  ***RXR***  .alpha. gene in adipocytes appeared to be
    without phenotype.

L4  ANSWER 2 OF 12  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
    1
AN  2002:310362  BIOSIS
DN  PREV200200310362
TI  Ligand-dependent genetic recombination in fibroblasts: A potentially
    powerful technique for investigating gene function in fibrosis.
AU  Zheng, Bing; Zhang, Zhaoping; Black, Carol M.; de Crombrugghe, Benoit;
    Denton, Christopher P. (1)
CS  (1) Center for Rheumatology, University College London, Rowland Hill St.,
    Royal Free Campus, London, NW3 2PF: c.denton@rfc.ucl.ac.uk UK
SO  American Journal of Pathology, (May, 2002) Vol. 160, No. 5, pp. 1609-1617.
    http://ajp.amjpathol.org/. print.
    ISSN: 0002-9440.
DT  Article
LA  English
AB  Strategies for conditional induction of  ***transgene***  expression in
    mice are likely to be valuable for testing the role of candidate genes in
    disease pathogenesis. We have developed a system for lineage-specific,
    ligand-dependent, induction of sustained  ***transgene***  expression in
    fibroblastic cells in mice using a chimeric gene encoding the  ***Cre***
    -  ***ER***  (T)  ***fusion***  protein, under the control of a
    fibroblast-specific regulatory sequence from the proalpha2(I)collagen
    gene. Cre-  ***ER***  (T) operates as a tamoxifen-dependent DNA
    recombinase to excise fragments flanked by specific LoxP consensus
    sequences. To test efficiency and ligand dependency of this strategy, Cre-
     ***ER***  (T)-expressing mice were backcrossed with heterozygous
    ROSA26-LacZ reporter mice, in which a floxed-STOP cassette has been
    introduced upstream of a bacterial beta-galactosidase (LacZ) reporter gene
    at a ubiquitously expressed locus. Constitutive or tamoxifen-induced LacZ
    expression was examined in embryonic, neonatal, and adult compound-
     ***transgenic***  mice. When pregnant ROSA26-LacZ females received a
    single dose of tamoxifen, high-level expression of LacZ in the skin was
    demonstrable from 24 hours after injection in double-  ***transgenic***
    embryos harboring both the Cre-  ***ER***  (T)  ***transgene***  and the
    target ROSA26-LacZ allele. High-level expression of LacZ was also induced
    postnatally by tamoxifen specifically in dermal and visceral fibroblasts.
    By allowing efficient embryonic or postnatal modification of alleles that
    have been targeted to incorporate LoxP sites, or to switch on
     ***transgenes***  cloned downstream of the floxed-STOP cassette, this
    system will allow fibroblast-specific genetic perturbations to be induced
    at predetermined embryonic or postnatal time points. This should greatly
    assist in in vivo functional studies of candidate genes in fibrotic
    diseases such as systemic sclerosis.

L4  ANSWER 3 OF 12  BIOSIS  COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
    2
AN  2002:298147  BIOSIS
DN  PREV200200298147
TI  Efficient recombination in diverse tissues by a tamoxifen-inducible form
    of Cre: A tool for temporally regulated gene activation/inactivation in
    the mouse.
AU  Hayashi, Shigemi; McMahon, Andrew P. (1)
CS  (1) Department of Molecular and Cellular Biology, Harvard University, 16
    Divinity Avenue, Cambridge, MA, 02138: amcmahon@mcb.harvard.edu USA
SO  Developmental Biology, (April 15, 2002) Vol. 244, No. 2, pp. 305-318.
    http://www.academicpress.com/db. print.
    ISSN: 0012-1606.
DT  Article
LA  English
AB  In recent years, the Cre integrase from bacteriophage P1 has become an
    essential tool for conditional gene activation and/or inactivation in
    mouse. In an earlier report, we described a  ***fusion***  protein
    between  ***Cre***  and a mutated form of the ligand binding domain of
    the estrogen receptor (Cre-ERTM) that renders Cre activity tamoxifen (TM)
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inducible, allowing for conditional modification of gene activity in the mammalian neural tube in utero. In the current work, we have generated a ***transgenic*** mouse line in which Cre-ERTM is ubiquitously expressed to permit temporally regulated Cre-mediated recombination in diverse tissues of the mouse at embryonic and adult stages. We demonstrate that a single, intraperitoneal injection of TM into a pregnant mouse at 8.5 days postcoitum leads to detectable recombination in the developing embryo within 6 h of injection and efficient recombination of a reporter gene in derivatives of all three germ layers within 24 h of injection. In addition, by varying the dose of TM injected, the percentage of cells undergoing a recombination event in the embryo can be controlled. Dose-dependent excision induced by TM was also possible in diverse tissues in the adult mouse, including the central nervous system, and in cultured cells derived from the ***transgenic*** mouse line. This inducible Cre system will be a broadly useful tool to modulate gene activity in mouse embryos, adults, and culture systems where temporal control is an important consideration.

L4 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 2003:35107 BIOSIS
DN PREV200300035107
TI ***ER*** -based double iCre fusion protein allows partial recombination in forebrain.
AU Casanova, Emilio (1); Fehsenfeld, Sandra; Lemberger, Thomas; Shimshek, Derya R.; Sprengel, Rolf; Mantamadiotis, Theo
CS (1) Abteilung Molekularbiologie der Zelle I., Deutsches Krebsforschungszentrum (DKFZ), Im Neuenheimer Feld 280, D-69120, Heidelberg, Germany: e.casanova@dkfz.de Germany
SO Genesis The Journal of Genetics and Development, (November 2002, 2002) Vol. 34, No. 3, pp. 208-214. print.
ISSN: 1526-954X.
DT Article
LA English
AB Here we describe the generation of a new tamoxifen-inducible double ***Cre*** ***fusion*** protein generated by fusing two ERT2 domains onto both ends of the iCre recombinase (a codon improved ***Cre*** recombinase). This ***Cre*** ***fusion*** protein (ERiCreER) had a twofold increased activity in cell culture assays than the previously described MerCreMer ***Cre*** double ***fusion*** protein. ERiCreER was targeted to the brain by placing it under the control of the promoter from the CamKIIalpha gene using a 170 kb BAC. The fusion protein was detected in hippocampus, cortex, striatum, thalamus, and hypothalamus but not in cerebellum. The ERiCreER was cytoplasmatic in the absence of tamoxifen and translocated into the nucleus upon tamoxifen administration. The activity of the ERiCreER was tested in vivo by mating the CamKIIalpha ERiCreER ***transgenic*** line with mice harbouring exon 10 of the CREB gene flanked by two LoxP sites. In the absence of tamoxifen, no background activity was detected in mice older than 6 months. After tamoxifen administration, most if not all of the ERiCreER fusion protein translocated from the cytoplasm to the nucleus; however, only 5-10% of the "floxed" CREB allele was recombined. Recombination was also visualised at the cellular level by following the upregulation of the CREM protein, which corresponds precisely with CREB loss/recombination. Unlike in other tissues (Sohal et al., 2001; Tannour-Louet et al., 2002), it appears that in brain, although ERiCreER can bind tamoxifen, the Cre-recombinase cannot be fully activated.

L4 ANSWER 5 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2002311838 EMBASE
TI Temporal Cre-mediated recombination exclusively in endothelial cells using Tie2 regulatory elements.
AU Forde A.; Constien R.; Grone H.-J.; Hammerling G.; Arnold B.
CS B. Arnold, Department of Molecular Immunology, Division of Tumor Immunology, German Cancer Research Center, Heidelberg 69120, Germany. b.arnold@dkfz-heidelberg.de
SO Genesis, (2002) 33/4 (191-197).
Refs: 21
ISSN: 1526-954X CODEN: GNESFY
CY United States
DT Journal; Article
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
AB The versatility of the bacteriophage Cre/LoxP system is dependent on the availability of a spectrum of tissue-specific Cre ***transgenic*** mice to address a host of biological questions. In this paper, we report on the generation of an inducible Tie2Cre ***transgenic*** mouse line that facilitates gene targeting exclusively in endothelial cells. The temporal manner of recombination is feasible through the use of a ***Cre*** -estrogen receptor ***fusion*** protein ***ER*** (T2) and was, in practical terms, achieved by feeding the animals the estrogen antagonist tamoxifen orally for 5 weeks. High efficiency of recombination was found in the vast majority of endothelial cell populations examined, as monitored by an EGFP reporter mouse line. Critically, no EGFP expression was observed in any uninduced mice. This inducible Cre line will be a very beneficial asset to investigating the role of endothelial specific genes in the adult mouse and to induce ***transgenes*** in the endothelium in an extremely efficient manner. .COPYRGT. 2002 Wiley-Liss, Inc.

L4 ANSWER 6 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 2001099876 EMBASE
TI An efficient system for conditional gene expression in embryonic stem cells and in their in vitro and in vivo differentiated derivatives.
AU Vallier L.; Mancip J.; Markossian S.; Lukaszewicz A.; Dehay C.; Metzger D.; Chambon P.; Samarut J.; Savatier P.
CS P. Savatier, Lab. de Biol. Moleculaire/Cellulaire, Ctr. Natl. de la Rech. Scientifique, Inst. Natl. Rech. Agronomique LA913, 46 Allee d'Italie, 69364 Lyon Cedex 07, France. Pierre.Savatier@ens-lyon.fr
SO Proceedings of the National Academy of Sciences of the United States of America, (27 Feb 2001) 98/5 (2467-2472).
Refs: 32
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 004 Microbiology
021 Developmental Biology and Teratology
037 Drug Literature Index
LA English
SL English
AB We have developed a universally applicable system for conditional gene expression in embryonic stem (ES) cells that relies on tamoxifen-dependent Cre recombinase-loxP site-mediated recombination and bicistronic gene-trap expression vectors that allow ***transgene*** expression from endogenous cellular promoters. Two vectors were introduced into the genome of recipient ES cells, successively: (i) a bicistronic gene-trap vector encoding the .beta.-galactosidase/neo(R) ***fusion*** protein and the ***Cre*** - ***ER*** (T2) (***Cre*** recombinase ***fused*** to a mutated ligand-binding domain of the human estrogen receptor) and (ii) a bicistronic gene-trap vector encoding the hygro(R) protein and the human alkaline phosphatase (hAP), the expression of which is prevented by tandemly repeated stop-of-transcription sequences flanked by loxP sites. In selected clones, hAP expression was shown to be regulated accurately by 4'hydroxy-tamoxifen. Strict hormone-dependent expression of hAP was achieved (i) in vitro in undifferentiated ES cells and embryoid bodies, (ii) in vivo in virtually all the tissues of the 10-day-old chimeric fetus (after injection of 4'hydroxy-tamoxifen to foster mothers), and (iii) ex vivo in primary embryonic fibroblasts isolated from chimeric fetuses. Therefore, this approach can be applied to drive conditional expression of virtually any ***transgene*** in a large variety of cell types, both in vitro and in vivo.

L4 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2003 ACS
AN 2001:47713 CAPLUS
DN 135:147951
TI Impaired adipogenesis and lipolysis in the mouse upon selective ablation of the retinoid X receptor .alpha. mediated by a tamoxifen-inducible chimeric Cre recombinase (Cre-ERT2) in adipocytes
AU Imai, Takeshi; Jiang, Ming; Chambon, Pierre; Metzger, Daniel
CS Institut de Genetique et de Biologie Moleculaire et Cellulaire, Centre National de la Recherche Scientifique/Institut National de la Sante et de la Recherche Medicale/Universite Louis Pasteur, College de France, Illkirch, 67404, Fr.
SO Proceedings of the National Academy of Sciences of the United States of America (2001), 98(1), 224-228
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Retinoid X receptor .alpha. (***RXR*** .alpha.) is involved in multiple signaling pathways, as a heterodimeric partner of several nuclear receptors. To investigate its function in energy homeostasis, the authors have selectively ablated the ***RXR*** .alpha. gene in adipocytes of 4-wk-old ***transgenic*** mice by using the tamoxifen-inducible Cre-ERT2 recombination system. Mice lacking ***RXR*** .alpha. in adipocytes were resistant to dietary and chem. induced obesity and impaired in fasting-induced lipolysis. Our results also indicate that ***RXR*** .alpha. is involved in adipocyte differentiation. Thus, the data demonstrate the feasibility of adipocyte-selective temporally controlled gene engineering and reveal a central role of ***RXR*** .alpha. in adipogenesis, probably as a heterodimeric partner for peroxisome proliferator-activated receptor .gamma..
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2001:271557 BIOSIS
DN PREV200100271557
TI Site- and time-specific gene targeting in the mouse.
AU Metzger, Daniel; Chambon, Pierre (1)
CS (1) College de France, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, 67404, Illkirch Cedex, C.U. de Strasbourg France
SO Methods (Orlando), (May, 2001) Vol. 24, No. 1, pp. 71-80. print.
ISSN: 1046-2023.
DT Article
LA English
SL English
AB The efficient introduction of somatic mutations in a given gene, at a given time, in a specific cell type, will facilitate studies of gene function and the generation of animal models for human diseases. We have established a conditional site-specific recombination system in mice using a new version of the Cre/lox system. The ***Cre*** recombinase has been ***fused*** to a mutated ligand binding domain of the human estrogen receptor (***ER***), resulting in a tamoxifen-dependent Cre recombinase, Cre-ERT, that is activated by tamoxifen, but not by estradiol. ***Transgenic*** mice were generated expressing Cre-ERT under the control of a cytomegalovirus promoter. Administration of tamoxifen to these ***transgenic*** mice induced excision of a chromosomally integrated gene flanked by loxP sites in a number of tissues, whereas no excision could be detected in untreated animals. However, the efficiency of excision varied between tissues, and the highest level (apprx40%) was obtained in the skin. To determine the efficiency of excision mediated by Cre-ERT in a given cell type, Cre-ERT-expressing mice were crossed with reporter mice in which expression of Escherichia coli beta-galactosidase can be induced through Cre-mediated recombination. The efficiency and kinetics of this recombination were analyzed at the cellular level in the epidermis of 6- to 8-week-old double ***transgenic*** mice. Site-specific excision occurred within a few days of tamoxifen treatment in essentially all epidermis cells expressing Cre-ERT. These results indicate that cell-specific expression of Cre-ERT in ***transgenic*** mice can be used for efficient tamoxifen-dependent Cre-mediated recombination at loci containing loxP sites, to generate site-specific somatic mutations in a spatiotemporally controlled manner. This conditional site-specific recombination system should allow the analysis of ***knockout*** phenotypes that cannot be addressed by conventional gene targeting.

L4 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5
AN 2000:55232 BIOSIS
DN PREV200000055232
TI Temporally-controlled site-specific mutagenesis in the basal layer of the epidermis: Comparison of the recombinase activity of the tamoxifen-inducible Cre-ERT and Cre-ERT2 recombinases.
AU Indra, Arup Kumar; Warot, Xavier; Brocard, Jacques; Bornert, Jean-Marc; Xiao, Jia-Hao; Chambon, Pierre (1); Metzger, Daniel
CS (1) College de France, Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, 67404, Illkirch Cedex, C.U. de Strasbourg France
SO Nucleic Acids Research, (Nov. 15, 1999) Vol. 27, No. 22, pp. 4324-4327.

ISSN: 0305-1048.
DT Article
LA English
SL English
AB Conditional DNA excision between two LoxP sites can be achieved in the mouse using ***Cre*** -ERT, a ***fusion*** protein between a mutated ligand binding domain of the human estrogen receptor (***ER***) and the Cre recombinase, the activity of which can be induced by 4-hydroxy-tamoxifen (OHT), but not natural ***ER*** ligands. We have recently characterized a new ligand-dependent recombinase, Cre-ERT2, which was apprx4-fold more efficiently induced by OHT than Cre-ERT in cultured cells. In order to compare the in vivo efficiency of these two ligand-inducible recombinases to generate temporally-controlled somatic mutations, we have engineered ***transgenic*** mice expressing a LoxP-flanked (floxed) ***transgene*** reporter and either Cre-ERT or Cre-ERT2 under the control of the bovine keratin 5 promoter that is specifically active in the epidermis basal cell layer. No background recombinase activity could be detected, while recombination was induced in basal keratinocytes upon OHT administration. Interestingly, a dose-response study showed that Cre-ERT2 was apprx10-fold more sensitive to OHT induction than Cre-ERT.

L4 ANSWER 10 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1998:446923 BIOSIS
DN PREV199800446923
TI A chimeric Cre recombinase inducible by synthetic, but not by natural ligands of the glucocorticoid receptor.
AU Brocard, Jacques; Feil, Robert; Chambon, Pierre (1); Metzger, Daniel
CS (1) Institut de Genetique et de Biologie Moleculaire et Cellulaire, CNRS/INSERM/ULP, College de France, BP 163, C.U. de Strasbourg, 67404 Illkirch Cedex France
SO Nucleic Acids Research, (Sept. 1, 1998) Vol. 26, No. 17, pp. 4086-4090. ISSN: 0305-1048.
DT Article
LA English
AB We have developed a new ligand-dependent chimeric recombinase (***Cre*** -GRdex) by ***fusing*** the site-specific ***Cre*** recombinase to the ligand binding domain (LBD) of a mutant human glucocorticoid receptor (GRdex). The synthetic glucocorticoid receptor (GR) ligands dexamethasone, triamcinolone acetonide and RU38486 efficiently induce recombinase activity in F9 murine embryonal carcinoma cells expressing constitutively Cre-GRdex. In contrast, no recombinase activity was detected in the absence of ligand or in the presence of the natural GR ligands corticosterone, cortisol or aldosterone. Moreover, physiological concentrations of these natural GR ligands do not affect Cre-GRdex recombinase activity induced by dexamethasone. Thus, ,as previously shown using ***Cre*** -oestrogen receptor (***ER***) ***fusion*** proteins, ***Cre*** -GRdex might be useful for achieving loxP site-directed mutagenesis in cultured cells and spatio-temporally controlled somatic cell mutagenesis in ***transgenic*** mice.

L4 ANSWER 11 OF 12 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
AN 1998028039 EMBASE
TI Spatio-temporally controlled site-specific somatic mutagenesis in the mouse.
AU Brocard J.; Warot X.; Wendling O.; Messaddeq N.; Vonesch J.-L.; Chambon P.; Metzger D.
CS P. Chambon, Genetique/Biol. Molec./Cell. Inst., Centre National de la Recherche Sci., Universite Louis Pasteur, 67404 Illkirch-Cedex, France. igbmc@igbmc.u-strasbg.fr
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) 94/26 (14559-14563). Refs: 16
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 022 Human Genetics
029 Clinical Biochemistry
LA English
SL English
AB The efficient introduction of somatic mutations in a given gene, at a given time, in a specific cell type will facilitate studies of gene function and the generation of animal models for humans diseases. We have shown previously that conditional recombination-excision between two loxP sites can be achieved in mice by using the ***Cre*** recombinase ***fused*** to a mutated ligand binding domain of the human estrogen receptor (Cre- ***ER*** (T)), which binds tamoxifen but not estrogens. DNA excision was induced in a number of tissues after administration of tamoxifen to ***transgenic*** mice expressing Cre- ***ER*** (T) under the control of the cytomegalovirus promoter. However, the efficiency of excision varied between tissues, and the highest level (.simeq.40%) was obtained in the skin. To determine the efficiency of excision mediated by Cre- ***ER*** (T) in a given cell type, we have now crossed Cre- ***ER*** (T)-expressing mice with reporter mice in which expression of Escherichia coli .beta.-galactosidase can be induced through Cre-mediated recombination. The efficiency and kinetics of this recombination were analyzed at the cellular level in the epidermis of 6- to 8-week-old double ***transgenic*** mice. We show that site-specific excision occurred within a few days of tamoxifen treatment in essentially all epidermis cells expressing Cre- ***ER*** (T). These results indicate that cell-specific expression of Cre- ***ER*** (T) in ***transgenic*** mice can be used for efficient tamoxifen-dependent, Cre-mediated recombination at loci containing loxP sites to generate site-specific somatic mutations in a spatio-temporally controlled manner.

L4 ANSWER 12 OF 12 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
AN 1996:508445 BIOSIS
DN PREV199699230801
TI Ligand-activated site-specific recombination in mice.
AU Feil, R.; Brocard, J.; Mascrez, B.; Le Meur, M.; Metzger, D.; Chambon, P. (1)
CS (1) Inst. Genet. Biol. Mol. Cell., Centre Natl. Recherche Scientifique, Inst. Natl. Sante Recherche Medicale, Univ. Louis Pasteur, College France, BP 163, 67404 Illkrich-Cedex, Strasbourg France
SO Proceedings of the National Academy of Sciences of the United States of America, (1996) Vol. 93, No. 20, pp. 10887-10890. ISSN: 0027-8424.
DT Article
LA English
AB Current mouse gene targeting technology is unable to introduce somatic mutations at a chosen time and/or in a given tissue. We report here that conditional site-specific recombination can be achieved in mice using a new version of the Cre/lox system. The ***Cre*** recombinase has been ***fused*** to a mutated ligand-binding domain of the human estrogen receptor (***ER***) resulting in a tamoxifen-dependent Cre recombinase, Cre- ***ER*** -T, which is activated by tamoxifen, but not by estradiol. ***Transgenic*** mice were generated expressing Cre- ***ER*** -T under the control of a cytomegalovirus promoter. We show that excision of a chromosomally integrated gene flanked by loxP sites can be induced by administration of tamoxifen to these ***transgenic*** mice, whereas no excision could be detected in untreated animals. This conditional site-specific recombination system should allow the analysis of ***knockout*** phenotypes that cannot be addressed by conventional gene targeting.

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COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.06 48.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
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CA SUBSCRIBER PRICE 0.00 -1.30

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(FILE 'HOME' ENTERED AT 17:50:29 ON 04 JUN 2003)

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 17:50:37 ON 04 JUN 2003
L1 216 S CRE (3A) (FUS? OR LIGAT?)
L2 37 S L1 AND (RXR OR RAR OR ER)
L3 26 S L2 AND (TRANSGEN? OR KNOCKOUT)
L4 12 DUP REM L3 (14 DUPLICATES REMOVED)

FILE 'STNGUIDE' ENTERED AT 17:56:54 ON 04 JUN 2003

FILE 'BIOSIS, EMBASE, CAPLUS' ENTERED AT 17:57:44 ON 04 JUN 2003

=> s l2 not l3
L5 11 L2 NOT L3

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 6 DUP REM L5 (5 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 2003:198022 BIOSIS
DN PREV200300198022
TI A noninvasive genetic/pharmacologic strategy for visualizing cell morphology and clonal relationships in the mouse.
AU Badea, Tudor C.; Wang, Yanshu; Nathans, Jeremy (1)
CS (1) Johns Hopkins University School of Medicine, 725 North Wolfe Street, 805 Preclinical Teaching Building, Baltimore, MD, 21205, USA: jnathans@jhmi.edu USA
SO Journal of Neuroscience, (March 15 2003) Vol. 23, No. 6, pp. 2314-2322. print.
ISSN: 0270-6474.
DT Article
LA English
AB Analysis of cellular morphology is the most general approach to neuronal classification. With the increased use of genetically engineered mice, there is a growing need for methods that can selectively visualize the morphologies of specified subsets of neurons. This capability is needed both to define cell morphologic phenotypes and to mark cells in a noninvasive manner for lineage studies. To this end, we describe a bipartite genetic system based on a ***Cre*** -estrogen receptor (***ER***) ***fusion*** protein that irreversibly activates a plasma membrane-bound alkaline phosphatase reporter gene by site-specific recombination. Because the efficiency and timing of gene rearrangement is controlled pharmacologically, a sparse subset of labeled cells can be generated from the set of CreER-expressing cells at any time during development. Histochemical visualization of alkaline phosphatase activity reveals neuronal morphology with strong and uniform labeling of all processes.

L6 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:365138 BIOSIS
DN PREV200000365138
TI Temporally-controlled site-specific mutagenesis in the adult mouse brain.
AU Weber, P. (1); Metzger, D. (1); Chambon, P. (1)

CS (1) IGBMC, Illkirch France
SO European Journal of Neuroscience, (2000) Vol. 12, No. Supplement 11, pp. 172. print.
Meeting Info.: Meeting of the Federation of European Neuroscience Societies Brighton, UK June 24-28, 2000
ISSN: 0953-816X.
DT Conference
LA English
SL English

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1999:299609 BIOSIS
DN PREV199900299609
TI Competition by exogenous estrogen receptor (***ER***) ligand binding domain results in leakiness from a ***Cre*** - ***ER*** ***fusion*** protein.
AU Gardner, Thomas W. (1); Harrison, David J. (1); Clarke, Alan R. (1)
CS (1) CRC Laboratories, Department of Pathology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SO Journal of Pathology, (1999) Vol. 187, No. SUPPL., pp. 23A.
Meeting Info.: 178th Meeting of the Pathological Society of Great Britain and Ireland Cambridge, England, UK January 6-8, 1999 Pathological Society of Great Britain and Ireland
. ISSN: 0022-3417.
DT Conference
LA English

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN 1997:211268 CAPLUS
DN 126:196099
TI Helper viruses containing recombination sites flanking a gene necessary for viral propagation and their use for preparing recombinant replication-deficient viral vectors
IN Lusky, Monika; Mehtali, Majid
PA Transgene S.A., Fr.; Lusky, Monika; Mehtali, Majid
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9705255	A2	19970213	WO 1996-FR1200	19960730
WO 9705255	A3	19970306		
W: AU, CA, JP, SG, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2737501	A1	19970207	FR 1995-9289	19950731
FR 2737501	B1	19971024		
CA 2225551	AA	19970213	CA 1996-2225551	19960730
AU 9667044	A1	19970226	AU 1996-67044	19960730
AU 715487	B2	20000203		
EP 842279	A2	19980520	EP 1996-927107	19960730
EP 842279	B1	20011031		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510049	T2	19990907	JP 1996-507291	19960730
EP 1132478	A2	20010912	EP 2001-108475	19960730
EP 1132478	A3	20020904		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 207959	E	20011115	AT 1996-927107	19960730
ES 2164910	T3	20020301	ES 1996-927107	19960730
US 6066478	A	20000523	US 1998-11257	19980309
US 6350575	B1	20020226	US 2000-563239	20000502
US 2002072120	A1	20020613	US 2001-920932	20010803
PRAI FR 1995-9289	A	19950731		
EP 1996-927107	A3	19960730		
WO 1996-FR1200	W	19960730		
US 1998-11257	A1	19980309		
US 2000-563239	A1	20000502		

AB Novel helper vectors are provided for complementing defective recombinant viral vectors, characterized in that they are provided with recombination sequences recognized by a recombinase. A complementation cell expressing the recombinase, and a method for prepg. recombinant viral vectors as infectious viral particles for transferring and expressing genes of interest in a host organism or cell, are also provided. THe invention is particularly suitable for use in gene therapy, esp. in humans. Adenoviral vector pTG4707 contg. an encapsidation signal flanked by loxP sites and lacking genes E1, E3 and E4 was constructed. Complementing cells 293/CRE-***ER*** , which are 293 cells transformed with a plasmid expressing an estradiol receptor- ***Cre*** recombinase ***fusion*** protein were also prepd. 293/CRE- ***ER*** cells transfected with pTG4707 and an E4-contg. retroviral vector are cultured to produce a mixed population of viral particles. Estradiol is then introduced into the medium to activate the Cre recombinase and inhibit formation of viral particles. Viral vectors enriched in the desired vectors, i.e. contg. fewer helper viruses relative to prior art viral vector prepns., are obtained.

L6 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1997:452452 BIOSIS
DN PREV199798751655
TI Regulation of Cre recombinase activity by mutated estrogen receptor ligand-binding domains.
AU Feil, Robert; Wagner, Juergen; Metzger, Daniel; Chambon, Pierre (1)
CS (1) Inst. Genetique Biol. Mol. Cell., CNRS/INSERM/ULP, Coll. France, BP 163, 67404 Illkirch-Cedex, C.U. de Strasbourg France
SO Biochemical and Biophysical Research Communications, (1997) Vol. 237, No. 3, pp. 752-757.
ISSN: 0006-291X.
DT Article
LA English
AB Ligand-dependent chimeric Cre recombinases are powerful tools to induce specific DNA rearrangements in cultured cells and in mice. We report here the construction and characterization of a series of chimeric recombinases, each consisting of ***Cre*** ***fused*** to a mutated human oestrogen receptor (***ER***) ligand-binding domain (LBD). Two new ligand-dependent recombinases which contain either the G400V/M543A/L544A or the G400V/L539A/L540A triple mutation of the human ***ER*** LBD are efficiently induced by the synthetic ***ER*** antagonists 4-hydroxytamoxifen (OHT) and ICI 182,780 (ICI), respectively, but are insensitive to 17-beta-oestradiol (E2). Both chimeric recombinases should be useful for efficient spatio-temporally controlled site-directed somatic mutagenesis.

L6 ANSWER 6 OF 6 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1995:408417 BIOSIS
DN PREV199598422717
TI Conditional site-specific recombination in mammalian cells using a ligand-dependent chimeric Cre recombinase.
AU Metzger, Daniel; Clifford, John; Chiba, Hideki; Chambon, Pierre
CS Inst. de Genet. et de Biologie Moleculaire et Cellulaire, Cent. Natl. de la Recherche Sci., Inst. Natl. de la Sante et de la Recherche Med., Universite Louis Pasteur, Coll. de France, 67404 Illkirch-Cedex, C.U. de Strasbourg France
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 15, pp. 6991-6995.
ISSN: 0027-8424.
DT Article
LA English
AB We have developed a strategy to generate mutant genes in mammalian cells in a conditional manner by employing a ***fusion*** protein, ***Cre*** - ***ER*** , consisting of the loxP site-specific Cre recombinase linked to the ligand-binding domain of the human estrogen receptor. We have established homozygous retinoid X receptor alpha-negative (***RXR*** -alpha-/-) F9 embryonal carcinoma cells constitutively expressing Cre- ***ER*** and have shown that estradiol or the estrogen agonist/antagonist 4-hydroxytamoxifen efficiently induced the recombinase activity, whereas no activity was detected in the absence of ligand or in the presence of the antiestrogen ICI 164,384. Furthermore, using a targeting vector containing a selection marker flanked by loxP sites, we have inactivated one retinoic acid receptor a allele in such a line, demonstrating that the presence of the recombinase does not inhibit homologous recombination. Combining this conditional site-specific recombination system with tissue-specific expression of Cre- ***ER*** may allow modification of the mammalian genome in vivo in a spatiotemporally regulated manner.

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CA SUBSCRIBER PRICE		-0.65	-1.95

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FULL ESTIMATED COST		0.12	64.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	ENTRY	SINCE FILE SESSION	TOTAL
CA SUBSCRIBER PRICE		0.00	-1.95

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NEWS 8 Sep 16 Experimental properties added to the REGISTRY file
NEWS 9 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 10 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 11 Oct 24 BEILSTEIN adds new search fields
NEWS 12 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 13 Nov 18 DKILIT has been renamed APOLLIT
NEWS 14 Nov 25 More calculated properties added to REGISTRY
NEWS 15 Dec 04 CSA files on STN
NEWS 16 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17 Dec 17 TOXCENTER enhanced with additional content
NEWS 18 Dec 17 Adis Clinical Trials Insight now available on STN
NEWS 19 Jan 29 Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20 Feb 13 CANCERLIT is no longer being updated
NEWS 21 Feb 24 METADEX enhancements

results in an increase in liver peroxisome number, marked hepatomegaly and induction of several genes encoding peroxisomal and other microsomal and mitochondrial enzymes involved in fatty acid metabolism. Chronic treatment of rodents with PP results in hepatocellular carcinoma. Species differences in PP responses have been found. For example, PP such as ciofibrate and gemfibrozil, are highly effective lipid and cholesterol lowering drugs in humans but do not cause peroxisome proliferation and there is no evidence for increased liver cancers in patients receiving these drugs. A receptor, designated PP-activated receptor alpha (PPAR-alpha) is capable of trans-activating reporter genes containing a PP response (PPRE), but requires the presence of both PP, 9-cis retinoic acid and another receptor called ***RXR*** - ***alpha*** . However, PP may not directly bind to PPAR-alpha but probably indirectly disturb cellular metabolism to liberate an endogenous ligand. Subsequent to the first identification of a PPAR-alpha, other members of this receptor family were found and designated PPAR-alpha, PPAR-beta (also called NUC1 and PPAR-delta) and PPAR-gamma. The alpha form is most abundant in liver and kidney, sites of peroxisome proliferation while the other two receptors are not significantly expressed in these tissues. On the basis of tissue-specific localization and spectrum of target gene activation, the physiological function of PPAR-alpha and PPAR-gamma appear to be related to fatty acid metabolism and regulation of ***adipogenesis*** , respectively. To gain insight into the function of PPAR-alpha and its role in the peroxisome proliferator response and hepatocellular carcinogenesis, gene targeting was used to develop a PPAR-alpha-deficient mouse. These animals are resistant to the pleiotropic effects of PP and no induction of any known target gene has been found. Recent studies on the phenotypes of these mice have led to an understanding of the mechanism of action of PP. They have also provided a useful model to establish the physiological role of PPAR-alpha in fatty acid homeostasis and inflammation.

L6 ANSWER 5 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:346448 BIOSIS
DN PREV199799645651
TI Decreased expression of murine PPAR-gamma in ***adipose*** tissue during endotoxemia.
AU Hill, Molly R.; Young, Misty D.; McCurdy, Caren M.; Gimble, Jeffrey M.
CS Dep. Radiologic Technology, Univ. Okla. Health Sciences Cent., 801 NE 13th Street, Oklahoma City, OK 73190 USA
SO Endocrinology, (1997) Vol. 138, No. 7, pp. 3073-3076.
ISSN: 0013-7227.
DT Article
LA English
AB Infection-induced hyperlipidemia develops due to a combination of factors, one of which is decreased clearance of lipids from the bloodstream due to depressed synthesis of lipoprotein lipase (LPL). Recently, the peroxisome proliferator activated receptors (PPARs) have been shown to be important in the regulation of LPL, particularly PPAR-gamma. PPAR-gamma and its heterodimerization partner, ***RXR*** - ***alpha*** have been shown to be transcriptional activators of LPL in co-transfection analysis. Therefore, we hypothesized that the decrease in LPL expression during endotoxemia may be a result of depressed PPAR-gamma expression. In these studies, we examined the effect of endotoxin or its proximal mediator, tumor necrosis factor (TNF), on the expression of PPAR-gamma in white (WAT) and brown ***adipose*** tissue (BAT) in CD- 1 mice. We report that treatment with endotoxin, but not TNF, transiently decreased PPAR-gamma mRNA levels 4 hr after treatment. However, endotoxin or TNF treatment decreased PPAR-gamma protein levels after 18 hr, which was at a time when LPL mRNA levels were also depressed. These data suggest that decreased PPAR-gamma expression following endotoxin or TNF treatment may contribute to the hyperlipidemia due to decreased expression of LPL, which would impair triglyceride clearance.

L6 ANSWER 6 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:185734 BIOSIS
DN PREV199799484937
TI Differential PPAR-gamma-2 and ***RxR*** - ***alpha*** expression in the differentiating 3T3-L1 ***adipocyte*** .
AU Thuillier, Philippe; Baillie, Rebecca; Clarke, Steven D.
CS Univ. Texas, Austin, TX 78712 USA
SO FASEB Journal, (1997) Vol. 11, No. 3, pp. A353.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology 97 New Orleans, Louisiana, USA April 6-9, 1997
ISSN: 0892-6638.
DT Conference; Abstract
LA English

L6 ANSWER 7 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:70483 BIOSIS
DN PREV199799369686
TI Terminal differentiation of human liposarcoma cells induced by ligands for peroxisome proliferator-activated receptor gamma and the retinoid X receptor.
AU Tontonoz, Peter (1); Singer, Samuel; Forman, Barry M.; Sarraf, Pasha; Fletcher, Jonathan A.; Fletcher, Christopher D. M.; Brun, Regina P.; Mueller, Elisabetta; Altiok, Soner; Oppenheim, Heather; Evans, Ronald M.; Spiegelman, Bruce M.
CS (1) Gene Expression Lab., The Salk Inst. Biological Studies, La Jolla, CA 92037 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 1, pp. 237-241.
ISSN: 0027-8424.
DT Article
LA English
AB Induction of terminal differentiation represents a promising therapeutic approach to certain human malignancies. The peroxisome proliferator-activated receptor gamma (PPAR-gamma) and the retinoid X receptor alpha (RX-R-alpha) form a heterodimeric complex that functions as a central regulator of ***adipocyte*** differentiation. Natural and synthetic ligands for both receptors have been identified. We demonstrate here that PPAR-gamma is expressed at high levels in each of the major histologic types of human liposarcoma. Moreover, primary human liposarcoma cells can be induced to undergo terminal differentiation by treatment with the PPAR-gamma ligand pioglitazone, suggesting that the differentiation block in these cells can be overcome by maximal activation of the PPAR pathway. We further demonstrate that RXR-specific ligands are also potent ***adipogenic*** agents in cells expressing the PPAR-gamma/ ***RXR*** - ***alpha*** heterodimer, and that simultaneous treatment of liposarcoma cells with both PPAR-gamma- and RXR-specific ligands results in an additive stimulation of differentiation. Liposarcoma cell differentiation is characterized by accumulation of intracellular lipid, induction of ***adipocyte*** -specific genes, and withdrawal from the cell cycle. These results suggest that PPAR-gamma ligands such as thiazolidinediones and RXR-specific retinoids may be useful therapeutic agents for the treatment of liposarcoma.

L6 ANSWER 8 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1996:364502 BIOSIS
DN PREV199699086858
TI A human peroxisome-proliferator-activated receptor-gamma is activated by inducers of ***adipogenesis*** , including thiazolidinedione drugs.
AU Lambe, Kevin G.; Tugwood, Jonathan D. (1)
CS (1) Res. Toxicol. Section, Zeneca Central Toxicology Lab., Alderley Park, Macclesfield, Cheshire SK10 4TJ UK
SO European Journal of Biochemistry, (1996) Vol. 239, No. 1, pp. 1-7.
ISSN: 0014-2956.
DT Article
LA English
AB We have cloned a human cognate of the mouse peroxisome-proliferator-activated receptor-gamma (hPPAR-gamma) from a human placenta cDNA library. Sequence analysis reveals a high degree of similarity with the mouse receptor and, like other PPAR, hPPAR-gamma forms heterodimers with the retinoid X receptor ***alpha*** (***RXR*** - ***alpha***) and binds in vitro to DNA elements containing direct repeats of the sequence TGACCT. In common with mouse PPAR-gamma, hPPAR-gamma is expressed strongly in ***adipose*** tissue, but significant levels also are detectable in placenta, lung and ovary. In vitro trans-activation data suggest hPPAR-gamma is only poorly activated by xenobiotic peroxisome proliferators, although certain fatty acids and eicosanoids are potent activators of this receptor. Both mouse and human PPAR-gamma are capable of being activated by thiazolidinedione drugs, although the two receptors appear to differ in their sensitivity to these compounds. Taken together, these data suggest a high degree of structural and functional similarity between mouse and human PPAR-gamma, and provide evidence for variation in human receptor structure which may result in differential sensitivity to activators.

L6 ANSWER 9 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1995:510753 BIOSIS
DN PREV199598515803
TI CDNA cloning and characterization of the transcriptional activities of the hamster peroxisome proliferator-activated receptor haPPAR-gamma.
AU Aperlo, Christel; Pognonec, Philippe; Saladin, Regis; Auwerx, Johan (1); Boulukos, Kim E.
CS (1) Inst. Pasteur Lille, 1 rue Calmettee, 59019 Lille France
SO Gene (Amsterdam), (1995) Vol. 162, No. 2, pp. 297-302.
ISSN: 0378-1119.
DT Article
LA English
AB We have isolated a cDNA corresponding to the hamster peroxisome proliferator-activated receptor haPPAR-gamma, a member of the steroid nuclear hormone receptor superfamily of transcription factors. haPPARγ mRNA is highly expressed in ***adipose*** tissue, and is expressed in lung, heart, kidney, liver and spleen to a lower extent. Thus, haPPARγ may function in activating the transcription of target genes in a variety of tissues, including those not particularly subjected to peroxisomal beta-oxidation. haPPAR-gamma binds efficiently in the presence of retinoid X receptor ***alpha*** (***RXR*** - ***alpha***) to a peroxisome proliferator response element (PPRE) first identified in the acyl-CoA oxidase (ACO) promoter, the rate-limiting enzyme of peroxisomal beta-oxidation. The gene (ACO) encoding this enzyme has been previously shown to be under the transcriptional control of mouse PPAR (mPPAR). Although binding of haPPAR-gamma/ ***RXR*** - ***alpha*** on the PPRE of the ACO promoter in vitro is similar to that observed for mPPAR/ ***RXR*** - ***alpha*** , we show that the transcriptional activities of mPPAR and haPPAR-gamma are regulated differently in vivo in response to peroxisome proliferators and heterodimerization with RXR.

L6 ANSWER 10 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1995:387777 BIOSIS
DN PREV199598402077
TI The combine effect of two transcription factors c/EBP- ***alpha*** and ***RXR*** /PPAR-gamma-2 stimulates ***adipogenesis*** in fibroblasts.
AU Vasseur-Cognet, Mireille
SO M-S (Medecine Sciences), (1995) Vol. 11, No. 4, pp. 625-626.
ISSN: 0767-0974.
DT Article
LA French

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.48	40.89

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.06	40.75

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NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25 Feb 26 PCTFULL now contains images
NEWS 26 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27 Mar 20 EVENTLINE will be removed from STN
NEWS 28 Mar 24 PATDPAFULL now available on STN
NEWS 29 Mar 24 Additional information for trade-named substances without structures available in REGISTRY
NEWS 30 Apr 11 Display formats in DGENE enhanced
NEWS 31 Apr 14 MEDLINE Reload
NEWS 32 Apr 17 Polymer searching in REGISTRY enhanced
NEWS 33 Apr 21 Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 34 Apr 21 New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 35 Apr 28 RDISCLOSURE now available on STN
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NEWS 37 May 15 MEDLINE file segment of TOXCENTER reloaded
NEWS 38 May 15 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39 May 18 CHEMREACT will be removed from STN
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NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation
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=> FIL BIOSIS EMBASE CAPLUS
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 0.21 0.21

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=> s adipo? and RXR
L1 324 ADIPO? AND RXR

=> s RXR (3a) alpha
L2 2709 RXR (3A) ALPHA

=> s adipo?
L3 125860 ADIPO?

=> s l3 and l2
L4 133 L3 AND L2

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 77 DUP REM L4 (56 DUPLICATES REMOVED)

=> s l5 and py<=2000
1 FILES SEARCHED...
L6 50 L5 AND PY<=2000

=> d bib abs

L6 ANSWER 1 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:335743 BIOSIS
DN PREV200000335743
TI A PPARgamma mutant serves as a dominant negative inhibitor of PPAR signaling and is localized in the nucleus.
AU Berger, Joel (1); Patel, Hansa V.; Woods, John; Hayes, Nancy S.; Parent, Stephen A.; Clemas, Joseph; Leibowitz, Mark D.; Elbrecht, Alex; Rachubinski, Richard A.; Capone, John P.; Moller, David E.
CS (1) Department of Molecular Endocrinology, Merck Research Laboratories, RY80N-C31, 126 E. Lincoln Avenue, Rahway, NJ, 07065 USA
SO Molecular and Cellular Endocrinology, (***April 25, 2000***) Vol. 162, No. 1-2, pp. 57-67. print.
ISSN: 0303-7207.
DT Article
LA English
SL English
AB The peroxisomal proliferator-activated receptors (PPARs) are members of the nuclear receptor superfamily that act as ligand-activated transcription factors. PPARgamma plays a critical role in regulating ***adipocyte*** differentiation and lipid metabolism. Recently, thiazolidinedione (TZD) and select non-TZD antidiabetic agents have been identified as PPARgamma agonists. To further characterize this receptor subclass, a mutant hPPARgamma lacking five carboxyl-terminal amino acids was produced (hPPARgamma2DELTA500). In COS-1 cells transfected with PPAR-responsive reporter constructs, the mutant receptor could not be activated by a potent PPARgamma agonist. When cotransfected with hPPARgamma2 or hPPARalpha, hPPARgamma2DELTA500 abrogated wild-type receptor activity in a dose-responsive manner. hPPARgamma2DELTA500 was also impaired with respect to binding of a high-affinity radioligand. In addition, its conformation was unaffected by normally saturating concentrations of PPARgamma agonist as determined by protease protection experiments. Electrophoretic mobility shift assays demonstrated that hPPARgamma2DELTA500 and hPPARgamma2 both formed heterodimeric complexes with human retinoid X receptor alpha (hRXRalpha) and could bind a peroxisome proliferator-responsive element (PPRE) with similar affinity. Therefore, hPPARgamma2DELTA500 appears to repress PPAR activity by competing with wild type receptor to dimerize with RXR and bind the PPRE. In addition, the mutant receptor may titrate out factors required for PPAR-regulated transcriptional activation. Both hPPARgamma2 and hPPARgamma2DELTA500 localized to the nucleus of transiently transfected COS-1 cells as determined by immunofluorescence using a PPARgamma-specific antibody. Thus, nuclear localization of PPARgamma occurs independently of its activation state. The dominant negative mutant, hPPARgamma2DELTA500, may prove useful in further studies to characterize PPAR functions both in vitro and in vivo

=> d bib abs 2

L6 ANSWER 2 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 2000:314239 BIOSIS
DN PREV200000314239
TI Sterol upregulation of human CETP expression in vitro and in transgenic mice by an LXR element.
AU Luo, Yi; Tall, Alan R. (1)
CS (1) Division of Molecular Medicine, Department of Medicine, Columbia University, New York, NY, 10032 USA
SO Journal of Clinical Investigation, (***February, 2000***) Vol. 105, No. 4, pp. 513-520. print.
ISSN: 0021-9738.
DT Article
LA English
SL English
AB The cholesterol ester transfer protein (CETP) facilitates the transfer of HDL cholesterol esters from plasma to the liver. Transgenic mice expressing human CETP, controlled by its natural flanking region, increase expression of this gene in response to hypercholesterolemia. We established a CETP promoter-luciferase reporter assay in differentiated 3T3-L1 ***adipocytes*** to map the sterol upregulatory element. Promoter mutagenesis suggested that a direct repeat of a nuclear receptor binding sequence separated by 4 nucleotides (DR4 element, -384 to-399) was responsible for this activity. Using mice carrying normal or mutated promoter sequences, we confirmed the importance of this element for gene induction by dietary sterol. A gel retardation complex containing LXR/RXR was identified using the CETP DR4 element and ***adipocyte*** nuclear extracts. Both LXRalpha/RXRalpha and LXRbeta/RXRalpha transactivated the CETP promoter via its DR4 element in a sterol-responsive fashion. Thus, the positive sterol response of the CETP gene is mediated by a nuclear receptor binding site that is activated by LXRs. That Cyp7a, the rate-limiting enzyme for conversion of cholesterol into bile acids in the liver, is also regulated by LXRalpha suggests that this class of nuclear receptor coordinates the regulation of HDL cholesterol ester catabolism and bile acid synthesis in the liver.

=> d bib abs 3

L6 ANSWER 3 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1998:492788 BIOSIS
DN PREV199800492788
TI A novel 3T3-L1 preadipocyte variant that expresses PPARgamma2 and RXRalpha but does not undergo differentiation.
AU Baillie, Rebecca A.; Sha, Xiaoming; Thuillier, Philippe; Clarke, Steven D. (1)
CS (1) Inst. Mol. Biol., Univ. Tex., Austin, TX 78712 USA
SO Journal of Lipid Research, (***Oct., 1998***) Vol. 39, No. 10, pp. 2048-2053.
ISSN: 0022-2275.
DT Article
LA English
AB This report describes a novel ***adipocyte*** -like cell line termed 3T3-L1/RB1 that was derived from preadipocyte cell line, 3T3-L1. The 3T3-L1/RB1 cells continued to divide after reaching confluence, formed foci, and constitutively expressed a low level of ***adipose*** fatty acid binding protein (A-FABP) mRNA. However, 3T3L-1/RB cells did not undergo terminal differentiation as indicated by the failure of insulin and thiazolidendiones to induce the expression of A-FABP, lipoprotein lipase, and fatty acid synthase. We hypothesized that the 3T3-L1/RB1 variant did not respond to differentiation stimuli because it did not express either peroxisomal proliferator activated receptor gamma2 (PPARgamma2) or its heterodimer partner, retinoid X receptor alpha (RXRalpha). Surprisingly, Western blots revealed that 3T3-L1/RB1 cells contained both PPARgamma2 and RXRalpha proteins at levels equal to or greater than that of the parent cell line. However, gel retardation assays using the ***adipose*** response element from A-FABP and nuclear protein extracts from 3T3-L1/RB1 cells treated with insulin or pioglitazone revealed that nuclear protein extracts from 3T3-L1/RB1 cells had very little ability to bind the PPARgamma2 recognition sequence of the A-FABP gene. These data suggest that the 3T3-L1/RB1 variant contains a mutation that may prevent ligand activation of PPARgamma2, and the subsequent conversion of 3T3-L1/RB1 cells to mature fat cells.

=> d bib abs 4-10

L6 ANSWER 4 OF 50 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
AN 1997:366218 BIOSIS
DN PREV199798658151
TI Recent update on the PPAR-alpha-null mouse.
AU Gonzalez, F. J.
CS Lab. Metabolism, Div. Basic Sci., Natl. Cancer Inst., Build. 37, Room 3E-24, NIH, Bethesda, MD 20892 USA
SO Biochimie (Paris), (1997) Vol. 79, No. 2-3, pp. 139-144.
ISSN: 0300-9084.
DT Journal; Article
LA English
AB Short-term treatment of rats and mice with peroxisome proliferators (PP)